

We claim:

1. A computer-implemented method for positioning a moveable item within a three-dimensional space observable under a microscope, the method comprising:
 - 5 presenting a graphical representation of at least a portion of the three-dimensional space;
 - receiving a user indication of a location within the graphical representation; and
 - 10 positioning the moveable item at a three-dimensional location in the three-dimensional space corresponding to the location within the graphical representation.
2. The method of claim 1 wherein positioning is performed responsive to receiving the user indication of the location within the graphical representation.
- 15 3. The method of claim 1 further comprising:
 - transforming the location on the graphical location to values indicating the three-dimensional location in the three-dimensional space.
- 20 4. The method of claim 3 wherein an implicit value is associated with the graphical location and transforming comprises:
 - calculating the values indicating the three-dimensional location via the implicit value.
- 25 5. The method of claim 4 wherein the implicit value is a focus location.
6. The method of claim 1 further comprising:
 - after positioning the moveable item, receiving an indication of a location within the graphical representation where the item appears.

7. The method of claim 6 further comprising:

after receiving an indication of a location within the graphical representation where the item appears, automatically interpreting a next indication of a location within the graphical representation as a directive for positioning the item at a three-dimensional location corresponding to the location indicated.

8. The method of claim 1 wherein the graphical representation is a captured image depicting a field of view of the microscope.

9. The method of claim 1 wherein the graphical representation is viewed through oculars of the microscope.

10. The method of claim 1 wherein the item is a microdelivery mechanism for delivering a pharmacological agent, the method further comprising:

after positioning the item at the three-dimensional location, delivering the pharmacological agent via the microdelivery mechanism at the three-dimensional location.

11. The method of claim 1 wherein positioning the item comprises directing the item with a micromanipulator via directives sent from a computer.

12. The method of claim 11 wherein positioning the item further comprises sending three-dimensional positioning information to a micromanipulator controller for the micromanipulator.

13. The method of claim 1 wherein the graphical representation of the three-dimensional space represents a region beneath the surface of a biological specimen being viewed under the microscope; and

positioning the item comprises directing the item beneath the surface of the biological specimen viewed under the microscope.

14. The method of claim 1 wherein the graphical representation of the three-dimensional space represents a portion of the three-dimensional space being viewed under the microscope at an objective magnification between 5x and 63x.

5 15. The method of claim 1 wherein the graphical representation of the three-dimensional space represents a portion of the three-dimensional space being viewed under the microscope at an objective magnification between 40x and 63x.

10 16. The method of claim 1 wherein the graphical representation of the three-dimensional space represents a portion of the three-dimensional space being viewed under the microscope at an objective magnification greater than or equal to 40x.

15 17. The method of claim 1 wherein receiving a user indication of a location within the graphical representation comprises receiving an activation of a graphical pointer positioned at a location on a presented image.

20 18. The method of claim 1 wherein presenting a graphical representation of the three-dimensional space comprises presenting a two-dimensional video representation of the three-dimensional space on a video display device.

25 19. The method of claim 1 wherein presenting a graphical representation of the three-dimensional space comprises presenting an image generated from observation of a portion of the three-dimensional space under a microscope.

30 20. The method of claim 19 wherein positioning the item at a three-dimensional location within the three-dimensional space comprises the following:
determining focus information indicating at what location the microscope is focused; and
transforming the location within the graphical representation and the focus information into information for directing the item to the three-dimensional location within the three-dimensional space.

21. The method of claim 20 further comprising:
defining a plurality of mathematical spaces; and
determining a point corresponding to the three-dimensional location within
5 the three-dimensional space by transforming a point from a first of the plurality of
mathematical spaces to an equivalent point in a second of the plurality of
mathematical spaces.
22. The method of claim 20 wherein transforming the location comprises:
10 transforming a three-dimensional location specified by a location within the
graphical representation and the focus information into a non-orthogonal coordinate
system for positioning the item at the three-dimensional location within the three-
dimensional space.
23. The method of claim 19 wherein
15 positioning the item at a three-dimensional location within the three-
dimensional space comprises the following:
determining depth information indicating at what depth the microscope is
focused;
20 transforming the location within the graphical representation and the depth
information into information in a coordinate system of a micromanipulator; and
sending the information in the coordinate system of the micromanipulator to
the micromanipulator.
24. The method of claim 23 wherein transforming the location comprises:
transforming a three-dimensional location specified by a location within the
graphical representation and the depth information into a non-orthogonal coordinate
system for directing the moveable item to the three-dimensional location within the
three-dimensional space, wherein the non-orthogonal coordinate system comprises a
30 declined axis.

25. The method of claim 1 wherein the three-dimensional space includes a biological specimen, which is viewed under the microscope; and

positioning the item comprises positioning the item with respect to the biological specimen viewed under the microscope.

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26. The method of claim 25 wherein the biological specimen is living.

27. The method of claim 25 wherein the biological specimen comprises brain tissue.

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28. The method of claim 25 wherein the biological specimen comprises nerve tissue.

29. The method of claim 25 wherein the biological specimen comprises muscle tissue.

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30. The method of claim 25 wherein the item is an electrode for measuring electrical signals.

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31. The method of claim 1 further comprising:

collecting information indicating a safe zone for an object, wherein the safe zone indicates a zone within which the item can be moved without damage to the object;

wherein positioning the item comprises directing the item to a location within the safe zone before positioning the item at the three-dimensional location.

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32. The method of claim 1 further comprising:

collecting information indicating a safe zone for an object under the microscope, wherein the safe zone indicates a zone within which the item can be moved without damage to the object; and

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responsive to an indication by the user, directing the item to a location within the safe zone.

33. The method of claim 32 wherein the safe zone is defined as a zone that is a specified distance above a stage of the microscope.

- 5 34. The method of claim 32 wherein the safe zone is defined as a zone that is a specified distance above a surface of the object.

35. The method of claim 1 further comprising:
determining an implicit z depth based on a z depth related to the graphical
10 representation of the portion of the three-dimensional space;
wherein positioning the item at a three-dimensional location within the
three-dimensional space comprises the following:
converting the implicit z depth and the indicated location within the
graphical representation into information in a three-dimensional coordinate system
15 specifying a physical location within the three-dimensional space; and
sending the information in the coordinate system specifying the physical
location within the three-dimensional space to a manipulator operable to move the
item to the physical location within the three-dimensional space.

- 20 36. The method of claim 35 further comprising:
converting the physical location within the three-dimensional space into a
three-dimensional coordinate system specifying the motor position of a motorized
manipulator.

- 25 37. The method of claim 35 further comprising:
collecting calibration information for the converting.

38. The method of claim 37 wherein collecting calibration information
comprises:
30 receiving a declination angle theta indicative of how far a drive axis for
manipulating the item is declined from horizontal.

39. The method of claim 37 wherein collecting calibration information comprises:

receiving a rotational angle ϕ indicative of how far a drive axis for manipulating the moveable item is rotated about a z axis.

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40. The method of claim 37 wherein collecting calibration information comprises:

generating a matrix for transforming a location within an image into a physical location within the three-dimensional space.

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41. The method of claim 40 wherein the matrix is a homogeneous matrix.

42. The method of claim 37 wherein collecting calibration information comprises:

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generating a matrix for transforming a physical location within the three-dimensional space into a motor position for a manipulator.

43. The method of claim 37 wherein collecting calibration information comprises:

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for a plurality of points, performing the following:
directing the item to a point; and
receiving an indication of where on the image the item appears.

44. The method of claim 37 wherein collecting calibration information comprises:

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for a plurality of points, performing the following:
under control of software, automatically directing the item to one of the points; and
receiving an indication of where on the image the item appears.

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45. The method of claim 44 wherein automatically directing comprises jogging the relative to the point and returning to the point under control of software.

46. The method of claim 37 wherein collecting calibration information comprises incrementally collecting calibration information.

5 47. The method of claim 37 wherein collecting calibration information comprises:

for a plurality of points observed at different focus positions of a microscope, performing the following:

directing the item to the point;

10 focusing the microscope so the item appears in focus;

receiving an indication of where on the image the item appears; and

collecting the focus position of the microscope.

15 48. The method of claim 47 wherein the item is the tip of an electrode.

49. A computer-implemented method for directing a probe via a micromanipulator to a three-dimensional location within a specimen observed under a microscope, the method comprising:

- capturing image data of the specimen from the microscope;
- 5 from the image data, generating a graphical image representing the specimen;
- presenting the graphical image representing the specimen;
- receiving an indication of a location on the graphical image, wherein the indication represents a location where the probe is to be moved;
- 10 determining a focus location indicative of where within the specimen the microscope is focussed;
- transforming the focus location and the location on the graphical image representing the specimen into a three-dimensional information for directing a micromanipulator to position the item at a corresponding location within the
- 15 specimen; and
- sending the three-dimensional information to the micromanipulator, whereby the item is positioned at a location within the specimen at a location corresponding to the location indicated on the graphical image representing the specimen.

20 50. A computer-readable medium comprising computer-executable instructions for positioning an item at a three-dimensional location with respect to a specimen observed under a microscope, the computer-readable medium comprising instructions for performing the following:

- presenting a graphical representation of the specimen on a display device;
- 25 receiving a user indication of a location within the graphical representation;
- and
- responsive to receiving the user indication of the location within the graphical representation, positioning the moveable item at a three-dimensional location with respect to the specimen corresponding to the location within the
- 30 graphical representation.

51. A computer-implemented system for positioning an item at a three-dimensional location within a specimen, the system comprising:

a graphical presentation of a two-dimensional representation of the specimen, wherein the graphical presentation is operable to receive an indication of
5 a location on the two-dimensional representation of the specimen;

a converter operable to convert the location on the two-dimensional representation of the specimen into three-dimensional information indicating the three-dimensional location within the specimen; and

a manipulation device operable to receive the three-dimensional information
10 indicating the three-dimensional location within the specimen to position the item at the three-dimensional location indicated by the three-dimensional information.

52. The computer-implemented system of claim 51 wherein the item is an electrode.

53. The computer-implemented system of claim 51 wherein the manipulation device is a micromanipulator.

54. The computer-implemented system of claim 51 further comprising:
20 one or more additional manipulation devices operable to receive the three-dimensional information indicating the three-dimensional location within the specimen to direct one or more additional items to the three-dimensional location indicated by the three-dimensional information.

55. The computer-implemented system of claim 51 wherein the two-dimensional representation of the specimen comprises an image depicting a field of view of a microscope.

56. The computer-implemented system of claim 55 wherein the
30 microscope is movable about a fixed stage.

57. A computer-implemented system for directing an item to a three-dimensional location within a specimen, the system comprising:

means for presenting a graphical representation of the specimen and accepting a user indication of a location within the graphical representation of the specimen;

means for directing the item to a specified three-dimensional location within the item; and

coupled to the means for presenting the graphical representation of the specimen and the means for directing the item, means for transforming the user indication of the location within the graphical representation of the specimen to a three-dimensional location within the item and operable to send the three-dimensional location to the means for directing the item to direct the item thereto.

58. The computer-implemented system of claim 57 wherein the graphical representation of the specimen is a representation of an image from a microscope, the system further comprising:

means for capturing the image from the microscope.